Complete Summary

GUIDELINE TITLE

Antithrombotic and thrombolytic therapy for ischemic stroke: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy.

BIBLIOGRAPHIC SOURCE(S)

Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):483S-512S. [202 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke. Chest 2001 Jan;119(1 Suppl):300S-320S.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Acute ischemic stroke
- Cerebral venous sinus thrombosis

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Family Practice
Internal Medicine
Neurology
Pulmonary Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To make recommendations for the use of antithrombotic and thrombolytic therapy in the management and treatment of ischemic stroke for the purpose of reducing mortality, disability, and complications of ischemic stroke
- To make recommendations for the use of antithrombotic therapy in the prevention of ischemic stroke

TARGET POPULATION

- Adults with or at risk of acute ischemic stroke
- Adults with cerebral venous sinus thrombosis

INTERVENTIONS AND PRACTICES CONSIDERED

Management/Treatment

Treatment of Acute Ischemic Stroke (AIS)

1. Thrombolytic therapy:
    - Intravenous (IV) recombinant tissue plasminogen activator (tPA) with strict adherence to eligibility criteria for use
    - In selected patients, intra-arterial thrombolytic therapy
2. Antithrombotic therapy:
    - Anticoagulation in selected patients
    - Early aspirin therapy
    - Aspirin therapy in combination with low doses of subcutaneous heparin

    Note: The following agents are considered but not recommended for the treatment of acute ischemic stroke: streptokinase (except within the confines of a clinical trial), full-dose anticoagulation, subcutaneous heparin and low-molecular-weight heparins or heparinoids.

Secondary Prevention of Deep Venous Thrombosis (DVT)/Pulmonary Embolism (PE) in Ischemic Stroke Patients

1. Low-dose subcutaneous heparin
2. Low-molecular-weight heparins
3. The heparinoid danaparoid
4. Nonpharmacologic measures:
    - Intermittent pneumatic compression devices
    - Elastic stockings

Prevention of Strokes

1. Aspirin therapy
2. Aspirin in combination with extended-release dipyridamole
3. Clopidogrel for patients allergic to aspirin

Note: Aspirin in combination with ticlopidine is considered, but not recommended.

Treatment of Cerebral Venous Sinus Thrombosis

1. Unfractionated heparin or low-molecular-weight heparin
2. Oral anticoagulation

Monitoring

1. International normalized ratio (INR)
2. Computed tomography (CT)
3. Magnetic resonance imaging (MRI)

MAJOR OUTCOMES CONSIDERED

Efficacy and safety of treatment, as defined by the following:

- Rates of mortality and disability from ischemic stroke
- Functional status
- Rates of deep vein thrombosis (DVT) and pulmonary embolism (PE) secondary to ischemic stroke
- Rates of adverse events from treatment, such as intracerebral hemorrhages (ICH)
- Relative risk reduction of recurrent stroke and other vascular events (prevention)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Process of Searching for Evidence

Defining the clinical question provided the framework for formulating eligibility criteria that guided the search for relevant evidence. Prior to searching for the evidence, methodological experts and librarians reviewed each question to ensure that the librarians could derive a comprehensive search strategy.

In specifying eligibility criteria, authors not only identified patients, interventions, and outcomes, but also methodological criteria. For most therapeutic studies, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, RCTs did not provide sufficient data, and article authors also included observational studies. This was also true when randomized trials were not the most appropriate design to use for addressing the research question. In particular, randomized trials are not necessarily the best design to understand risk groups (e.g., the baseline or expected risk of a given event for certain subpopulations). Because there are no interventions examined in questions about prognosis, one replaces interventions by the exposure, which is time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians at the University at Buffalo conducted comprehensive literature searches. For each question the authors provided, the librarians developed sensitive (but not specific) search strategies, including all languages, and conducted separate searches for systematic reviews, RCTs, and, if applicable, observational studies. The librarians searched the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness and Cochrane Register of Controlled Trial, the ACP Journal Club, MEDLINE, and Embase for studies published between 1966 and June 2002 in any language. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration (full strategy available in Appendix online at: http://www.chestjournal.org/content/vol126/3_suppl_1).

For observational studies, they restricted their searches to human studies. Searches were not further restricted in terms of methodology. While increasing the probability of identifying all published studies, this sensitive approach resulted in large number of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search and removed any apparently irrelevant citations. These irrelevant citations included press news, editorials, narrative reviews, single case reports, animal studies (any nonhuman studies), and letters to the editor. Authors included data from abstracts of recent meetings if reporting was transparent and all necessary data for the formulation of a recommendation were available. The guideline developers did not explicitly use Internet sources to search for research data.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) (and the methodological quality of the underlying evidence (A, B, C+, or C). See "Rating Scheme for the Strength of the Recommendations."

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Summarizing Evidence

The electronic searches also included searching for systematic reviews. If authors were satisfied with a recent high-quality systematic review, evidence from that review provided a foundation for the relevant recommendation.

Pooled analyses from high-quality systematic reviews formed, wherever possible, the evidence base of the recommendations. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for a greater generalizability of results. However, pooling also bears the risk of spurious generalization. In general, the summary estimates of interest were the different types of outcomes conveying benefit and downsides (i.e., risk, burden, and cost).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The strength of any recommendation depends on the following two factors: the trade-off between the benefits and the risks, burdens, and costs; and the strength of the methodology that leads to the treatment effect. The guideline developers grade the trade-off between benefits and risks in the two categories: 1, in which the trade-off is clear enough that most patients, despite differences in values, would make the same choice; and 2, in which the trade-off is less clear, and individual patients´ values will likely lead to different choices.

When randomized trials provide precise estimates suggesting large treatment effects, and the risks and costs of therapy are small, treatment for average patients with compatible values and preferences can be confidently recommended.

If the balance between benefits and risks is in doubt, methodologically rigorous studies providing Grade A evidence and recommendations may still be weak (Grade 2). Uncertainty may come from less precise estimates of benefit, harm, or costs, or from small effect sizes.

There is an independent impact of validity and consistency, and the balance of positive and negative impacts of treatment on the strength of recommendations. In situations in which there is doubt about the value of the trade-off, any recommendation will be weaker, moving from Grade 1 to Grade 2.

Grade 1 recommendations can only be made when there is a relatively clear picture of both the benefits and the risks, burdens, and costs, and when the balance between the two clearly favors recommending or not recommending the intervention for the typical patient with compatible values and preferences. A number of factors can reduce the strength of a recommendation, moving it from Grade 1 to Grade 2. Uncertainty about a recommendation to treat may be introduced if the following conditions apply: (1) the target event that is trying to be prevented is less important (confident recommendations are more likely to be made to prevent death or stroke than asymptomatic deep vein thrombosis); (2) the magnitude of risk reduction in the overall group is small; (3) the probability of the target event is low in a particular subgroup of patients; (4) the estimate of the treatment effect is imprecise, as reflected in a wide confidence interval (CI) around the effect; (5) there is substantial potential harm associated with therapy; or (6) there is an expectation for a wide divergence in values even among average or typical patients. Higher costs would also lead to weaker recommendations to treat.

The more balanced the trade-off between benefits and risks, the greater the influence of individual patient values in decision making. Virtually all patients, if they understand the benefits and risks, will take aspirin after experiencing a myocardial infarction (MI) or will comply with prophylaxis to reduce the risk of thromboembolism after undergoing hip replacement. Thus, one way of thinking about a Grade 1 recommendation is that variability in patient values is unlikely to influence treatment choice in average or typical patients.

When the trade-off between benefits and risks is less clear, individual patient values may influence treatment decisions even among patients with average or typical preferences.

Grade 2 recommendations are those in which variation in patient values or individual physician values will often mandate different treatment choices, even among average or typical patients. An alternative, but similar, interpretation is that a Grade 2 recommendation suggests that clinicians conduct detailed conversations with patients to ensure that their ultimate recommendation is consistent with the patient's values.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
1A	Clear	Randomized controlled trials (RCTs) without important limitations	Strong recommendation; can apply to most patients in most circumstances without reservation
1C+	Clear	No RCTs, but strong RCT results can be unequivocally extrapolated, or overwhelming evidence from observational studies	Strong recommendation; can apply to most patients in most circumstances
1B	Clear	RCTs with important limitations (inconsistent results, methodological flaws*)	Strong recommendation; likely to apply to most patients
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence is available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances or patients' or societal values
2C+	Unclear	No RCTs, but strong RCT results can be	Weak recommendation; best action may

Grade of Recommendation	Clarity of Risk/Benefit	Methodological Strength of Supporting Evidence	Implications
		unequivocally extrapolated, or overwhelming evidence from observational studies	differ depending on circumstances or patients' or societal values
2B	Unclear	RCTs with important limitations (inconsistent results, methodological flaws*)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

*These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.

COST ANALYSIS

While conference participants agreed that recommendations should reflect economic considerations, incorporating costs is fraught with difficult challenges. For most recommendations, formal economic analyses are unavailable. Even when analyses are available, they may be methodologically weak or biased. Furthermore, costs differ radically across jurisdictions, and even sometimes across hospitals within jurisdictions.

Because of these challenges, the guideline developers consider economic factors only when the costs of one therapeutic option over another are substantially different within major jurisdictions in which clinicians make use of these recommendations. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far better than some of the interventions that are designated as Grade 1A. This will likely be true for all less industrialized countries and, with the increasing promotion of expensive drugs with marginal benefits, may be increasingly true for wealthier nations. Furthermore, recommendations change (either in direction or with respect to grade) only when the guideline developers believe that costs are high

in relation to benefits. Instances in which costs have influenced recommendations are labeled in the "values and preferences" statements associated with the recommendation.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline authors formulated draft recommendations prior to the conference that served as the foundation for authors to work together and critique the recommendations. Drafts of all articles including draft recommendations were available for review during the conference. A representative of each article presented potentially controversial issues in their recommendations at plenary meetings. Article authors met to integrate feedback, to consider related recommendations in other articles, and to revise their own guidelines accordingly. Authors continued this process after the conference until they reached agreement within their groups and with other author groups who had provided critical feedback. Finally, the editors of this supplement harmonized the articles and resolved remaining disagreements through facilitated discussion.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The rating scheme is defined at the end of the "Major Recommendations" field.

Acute Ischemic Stroke (AIS): Thrombolytic Therapy in Acute Stroke

Intravenous (IV) Tissue Plasminogen Activator (tPA) for AIS within 3 hours of Symptom Onset

1. For eligible patients (see inclusion and exclusion criteria listed below), the guideline developers recommend administration of IV tPA in a dose of 0.9 mg/kg (maximum 90 mg), with 10% of the total dose administered as an initial bolus, and the remainder infused over 60 min, provided that treatment is initiated within 3 hours of clearly defined symptom onset (Grade 1A).

   Underlying values and preferences: This recommendation assumes a relatively higher value on long-term functional improvement and a relatively lower value on minimizing the risk of intracranial hematomas (ICH) in the immediate peristroke period.

2. For patients with extensive (more than one third of the middle cerebral artery [MCA] territory) and clearly identifiable hypodensity on CT, the guideline developers recommend against thrombolytic therapy (Grade 1B).

IV tPA for AIS between 3 to 6 hours of Symptom Onset

1. For unselected patients with AIS of >3 hours but <6 hours, the guideline developers suggest clinicians not use IV tPA (Grade 2A).

   Underlying values and preferences: This recommendation assumes a relatively low value on small increases in long-term functional improvement, a relatively high value on avoiding acute ICH and death, and a relatively high degree of risk aversion.

IV Streptokinase for AIS between 0 and 6 hours of Symptom Onset

1. For patients with AIS, the guideline developers recommend against streptokinase (Grade 1A).

Intra-Arterial Thrombolysis for AIS

1. For patients with angiographically demonstrated middle cerebral artery (MCA) occlusion and no signs of major early infarction on the baseline CT scan, who can be treated within 6 hours of symptom onset, the guideline developers suggest use of intra-arterial thrombolytic therapy with tPA (Grade 2C).
2. For patients with acute basilar artery thrombosis and without major CT/magnetic resonance imaging (MRI) evidence of infarction, the guideline developers suggest intra-arterial thrombolysis with tPA (Grade 2C).

AIS: Patients Not Eligible for Thrombolysis

Anticoagulants for Altering Outcomes among Acute Stroke in Patients Not Eligible for Thrombolysis

1. For patients with AIS, the guideline developers suggest clinicians not use full-dose anticoagulation with IV, subcutaneous, or low molecular weight heparin or heparinoids (Grade 2B).

Antiplatelet Agents for Altering Outcomes in Acute Stroke in Patients Not Eligible for Thrombolysis

1. For patients with ischemic stroke who are not receiving thrombolysis, the guideline developers recommend early aspirin therapy, 160 to 325 mg/day (Grade 1A).

Antithrombotic Therapy for Prevention of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) in AIS

1. For acute stroke patients with restricted mobility, the guideline developers recommend prophylactic low-dose subcutaneous heparin or low molecular weight heparins or heparinoids (Grade 1A).
2. For patients who have contraindications to anticoagulants, the guideline developers recommend use of intermittent pneumatic compression devices or elastic stockings (Grade 1C).

DVT/PE Prophylaxis in Patients with ICH

Heparin for DVT/PE Prophylaxis in Patients with ICH

1. In patients with an acute ICH, the guideline developers recommend the initial use of intermittent pneumatic compression (Grade 1C+). In stable patients, the guideline developers suggest low-dose subcutaneous heparin may be initiated as soon as the second day after the onset of the hemorrhage (Grade 2C).

   Underlying values and preferences: The recommendation for subcutaneous heparin assumes a relatively low degree of risk aversion.

Stroke Prevention

Prevention of Cerebral Ischemic Events in Patients with Noncardioembolic Transient Ischemic Attack (TIA) or Stroke: Antiplatelet Drugs vs. Placebo or vs. an Alternative Antiplatelet Drug

1. In patients who have experienced a noncardioembolic stroke or TIA (i.e., atherothrombotic, lacunar, or cryptogenic), the guideline developers recommend treatment with an antiplatelet agent (Grade 1A). Aspirin at a dose of 50 to 325 mg daily (qd); the combination of aspirin, 25 mg, and extended-release dipyridamole, 200 mg twice a day (bid); or clopidogrel, 75 mg qd, are all acceptable options for initial therapy.
2. In patients receiving aspirin who are at moderate-to-high risk of bleeding complications, the guideline developers recommend using low doses of aspirin, 50 to 100 mg/day (Grade 1C+).
3. In patients who have experienced a noncardioembolic stroke or TIA, the guideline developers suggest use of the combination of aspirin and extended-release dipyridamole, 25/200 mg bid, over aspirin (Grade 2A), and clopidogrel over aspirin (Grade 2B).

   Underlying values and preferences: This recommendation to use the combination of aspirin and extended-release dipyridamole or clopidogrel over aspirin places a relatively high value on a small absolute risk reduction in stroke rates, and a relatively low value on minimizing drug expenditures.

4. For patients who are allergic to aspirin, the guideline developers recommend clopidogrel (Grade 1C+).

Prevention of Noncardioembolic Cerebral Ischemic Events: Oral Anticoagulants

1. For most patients with noncardioembolic stroke or TIA, the guideline developers recommend antiplatelet agents over oral anticoagulation (Grade 1A).
2. For patients with well-documented prothrombotic disorders, the guideline developers suggest oral anticoagulation over antiplatelet agents (Grade 2C).

Prevention of Cerebral Ischemic Events in Patients Undergoing Carotid Endarterectomy: Antiplatelet Agents

1. In patients undergoing carotid endarterectomy, the guideline developers recommend aspirin, 81 to 325 mg/d, prior to and following the procedure (Grade 1A).

Prevention of Cardioembolic Cerebral Ischemic Events

Patients with Stroke with Underlying Atrial Fibrillation: Anticoagulation

1. In patients with atrial fibrillation who have had a recent stroke or TIA, the guideline developers recommend long-term oral anticoagulation (target INR, 2.5; range, 2.0 to 3.0) [Grade 1A].

Patients with Stroke with Underlying Atrial Fibrillation: Antiplatelet Agents

1. For patients with cardioembolic stroke who have contraindications to anticoagulant therapy, the guideline developers recommend aspirin (Grade 1A).

Patients with Aortic Atheromata

1. In patients with stroke associated with aortic atherosclerotic lesions, the guideline developers recommend antiplatelet therapy over no therapy (Grade 1C+). For patients with cryptogenic stroke associated with mobile aortic arch thrombi, the guideline developers suggest either oral anticoagulation or antiplatelet agents (Grade 2C).

Patients with Patent Foramen Ovale (PFO)

1. In patients with cryptogenic ischemic stroke and a patent foramen ovale, the guideline developers recommend antiplatelet therapy over no therapy (Grade 1C+), and suggest antiplatelet agents over anticoagulation (Grade 2A).

Mitral Valve Strands and Prolapse

1. In patients with mitral valve strands or prolapse, who have a history of TIA or stroke, the guideline developers recommend antiplatelet therapy (Grade 1C+).

Cerebral Venous Sinus Thrombosis

Anticoagulation for Cerebral Venous Sinus Thrombosis

1. In patients with venous sinus thrombosis, the guideline developers recommend that clinicians use unfractionated heparin (Grade 1B) or low molecular weight heparin (Grade 1B) over no anticoagulant therapy during the acute phase, even in the presence of hemorrhagic infarction. In these patients, the guideline developers recommend oral anticoagulation for 3 to 6 months (target INR, 2.5; range, 2.0 to 3.0) [Grade 1C].

Definitions

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2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

*These situations include RCTs with both lack of blinding and subjective outcomes, where the risk of bias in measurement of outcomes is high, or RCTs with large loss to follow-up.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Therapeutic strategies designed to restore cerebral perfusion in a timely fashion have the potential to limit the cellular, biochemical, and metabolic

consequences of cerebral ischemia that ultimately lead to irreversible brain injury.
- Appropriate use of antithrombotic and thrombolytic agents in ischemic stroke patients may reduce the rates and relative risk of ischemic stroke.

POTENTIAL HARMS

The primary risk of thrombolytic therapy is cerebral hemorrhage. In one study, symptomatic intracerebral hemorrhage occurred in 6.4% of patients receiving tissue plasminogen activator (tPA) versus 0.6% of the placebo-treated patients ($p < 0.001$). Despite the increased risk of hemorrhage, patients with severe strokes were more likely to have favorable outcomes if treated with tissue plasminogen activator (adjusted odds ratio, 4.3; 95% confidence interval, 1.6 to 11.9).

CONTRAINDICATIONS

CONTRAINDICATIONS

- Aspirin is contraindicated among those with aspirin allergy or those with active gastrointestinal (GI) bleeding.
- Thrombolytic therapy is contraindicated in patients with computed tomography (CT) signs of intracranial hematoma (ICH), a history of ICH, seizure at stroke onset, stroke or serious head injury within 3 months, major surgery or serious trauma within 2 weeks, gastrointestinal (GI) or urinary tract hemorrhage within 3 weeks, systolic blood pressure >185 mm Hg, diastolic blood pressure >110 mm Hg, aggressive treatment required to lower blood pressure (BP), glucose level < 50 mg/dL or >400 mg/dL, symptoms of subarachnoid hemorrhage, arterial puncture at a noncompressible site or lumbar puncture within 1 week, platelet count <100,000 platelets/microliters, heparin therapy within 48 hours associated with elevated activated partial thromboplastin time, clinical presentation suggesting post-myocardial infarction (MI) pericarditis, pregnant or lactating women, and current use of oral anticoagulants (prothrombin time > 15 seconds, international normalized ratio [INR] >1.7).
- For patients with extensive (more than one third of the middle cerebral artery [MCA] territory) and clearly identifiable hypodensity on computed tomography (CT), the guideline developers recommend against thrombolytic therapy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Interpreting the Recommendations

Clinicians, third-party payers, institutional review committees, or the courts should not construe these guidelines in any way as absolute dictates. In general, anything other than a Grade 1A recommendation indicates that the article authors acknowledge that other interpretations of the evidence, and other clinical policies, may be reasonable and appropriate. Even Grade 1A recommendations will not apply to all circumstances and all patients. For instance, the guideline developers have been conservative in their considerations of cost and have

seldom downgraded recommendations from Grade 1 to Grade 2 on the basis of expense. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far better than some of the interventions that are designated as Grade 1A. This will likely be true for all less industrialized countries and, with the increasing promotion of expensive drugs with marginal benefits, may be increasingly true for wealthier nations.

Similarly, following Grade 1A recommendations will at times not serve the best interests of patients with atypical values or preferences or of those whose risks differ markedly from those of the usual patient. For instance, consider patients who find anticoagulant therapy extremely aversive, either because it interferes with their lifestyle (e.g., prevents participation in contact sports) or because of the need for monitoring. Clinicians may reasonably conclude that following some Grade 1A recommendations for anticoagulation therapy for either group of patients will be a mistake. The same may be true for patients with particular comorbidities (e.g., a recent gastrointestinal bleed or a balance disorder with repeated falls) or other special circumstances (e.g., very advanced age) that put them at unusual risk.

The guideline developers trust that these observations convey their acknowledgment that no recommendations or clinical practice guidelines can take into account the often compelling and unique features of individual clinical circumstances. No clinician, and no body charged with evaluating a clinician´s actions, should attempt to apply these recommendations in a rote or blanket fashion.

Limitations of Guideline Development Methods

The limitations of these guidelines include the possibility that some authors followed this methodology more closely than others, although the development process was centralized and supervised by the editors. Second, it is possible that the guideline developers missed relevant studies despite the comprehensive searching process. Third, the guideline developers did not centralize the methodological evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines. Fourth, if high-quality meta-analyses were unavailable, the guideline developers did not statistically pool primary study results using meta-analysis. Finally, sparse data on patient preferences and values, resources, and other costs represent additional limitations that are inherent to most guideline development methods.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Guideline Implementation Strategies

A full review of implementation strategies for practice guidelines is provided in the companion document titled "Antithrombotic and Antithrombolytic Therapy: From Evidence to Application." The review suggests that there are few implementation strategies that are of unequivocal, consistent benefit, and that are clearly and consistently worth resource investment. The following is a summary of the

recommendations (see "Major Recommendations" for a definition of the recommendation grades).

To encourage uptake of guidelines, the guideline developers recommend that appreciable resources be devoted to distribution of educational material (Grade 2B).

They also suggest that:

- Few resources be devoted to educational meetings (Grade 2B)
- Few resources be devoted to educational outreach visits (Grade 2A)
- Appreciable resources be devoted to computer reminders (Grade 2A)
- Appreciable resources be devoted to patient-mediated interventions to encourage uptake of the guidelines (Grade 2B)
- Few resources be devoted to audit and feedback (Grade 2B)

IMPLEMENTATION TOOLS

Patient Resources
Personal Digital Assistant (PDA) Downloads
Quick Reference Guides/Physician Guides
Resources
Slide Presentation
Tool Kits

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):483S-512S. [202 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan (revised 2004 Sep)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

Funding was provided through an unrestricted educational grant by AstraZeneca LP, Aventis Pharmaceuticals, GlaxoSmithKline, Bristol-Myer Squibb/Sanofi-Synthelabo Partnership, and Organon Sanofi-Synthelabo LLC.

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American College of Chest Physicians Consensus Panel on Antithrombotic and Thrombolytic Therapy

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Albers has received research support and honoraria as a consultant from AstraZeneca, Bristol- Myers Squibb, Boehringer Ingelheim, Genentech and Sanofi-Arganon.

Dr. Easton has received honoraria for his participation on advisory boards or as a speaker at educational events from Boehringer Ingelheim, Bristol- Myers Squibb, and Sanofi-Synthelabo.

Dr. Sacco has received research funding from GlaxoSmithKline and Pfizer, and has received honoraria for his participation as a consultant on advisory boards, data and safety monitoring boards and/or as a speaker at educational events from Boehringer Ingelheim, sanofi-Synthelabo, Bristol-Myers Squibb, Pfizer, AstraZeneca, GlaxoSmithKline, and Texas Biotechnology.

Dr. Teal has received honoraria for participation on advisory boards and/or as a speaker at medical education events supported by Boehringer-Ingelheim, Sanofi-Synthelabo and Bayer, Servier, Aventis, PAION, AstraZeneca, and Hoffman-LaRoche. He has served on research steering committees for clinical trials conducted by Boehinger-Ingelheim, Bayer, ONO Pharmaceuticals and Pfizer and Eli-Lilly, EKOS, GlaxoSmithKline, and Yamaguichi.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Albers GW, Amarenco P, Easton JD, Sacco RL, Teal P. Antithrombotic and thrombolytic therapy for ischemic stroke. Chest 2001 Jan;119(1 Suppl):300S-320S.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Evidence-based guidelines. Northbrook, IL: ACCP, 2004 Sep.
- Methodology for guideline development for the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Applying the grades of recommendation for antithrombotic and thrombolytic therapy: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Hemorrhagic complications of anticoagulant treatment: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Antithrombotic and thrombolytic therapy: from evidence to application: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.
- Platelet-active drugs: the relationships among dose, effectiveness, and side effects: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Northbrook, IL: ACCP, 2004 Sep.

Electronic copies: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.

Print copies: Available from the American College of Chest Physicians (ACCP), Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

The following is also available:

- Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence-based guidelines; quick reference guide. Northbrook, IL: ACCP, 2004 Sep. Personal Digital Assistant (PDA) download available at ACCP Web site.

Additional implementation tools are also available:

- Clinical resource: antithrombotic and thrombolytic therapy. Northbrook, IL. ACCP, 2004. Ordering information: Available from the ACCP Web site.

PATIENT RESOURCES

The following is available:

- A patient's guide to antithrombotic and thrombolytic therapy. In: Clinical resource: antithrombotic and thrombolytic therapy. Northbrook (IL): American College of Chest Physicians (ACCP). 2004.

Ordering information is available from the ACCP Web site.

advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on July 30, 2001. The information was verified by the guideline developer on September 27, 2001. This NGC summary was updated by ECRI on December 9, 2004. The updated information was verified by the guideline developer on January 12, 2005.

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Date Modified: 5/16/2005